IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATERA, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. _____
	)	
INIVATA, INC. and INIVATA LTD.,	)	**JURY TRIAL DEMANDED**
	)	
Defendants.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Natera, Inc. ("Natera") submits this Complaint against Defendants Inivata, Inc. and Inivata Ltd. and (collectively, "Inivata" or "Defendants"), and alleges as follows:

OVERVIEW OF THE ACTION

1. This action arises under the patent laws of the United States, 35 U.S.C. §§ 1, *et seq.*, from Inivata's infringement of Natera's U.S. Patent Nos. 10,262,755 (the "'755 patent") and 10,597,709 (the "'709 patent") (collectively, the "Asserted Patents").

THE PARTIES

2. Plaintiff Natera is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business at 201 Industrial Road, San Carlos, California 94070.

3. Founded in 2004, Natera (f.k.a. Gene Security Network) is a pioneering molecular technology company with industry-leading healthcare diagnostics products. Natera is dedicated to improving disease management for oncology, reproductive health, and organ transplantation. For well over a decade, Natera has been researching and developing non-invasive methods for analyzing DNA in order to help patients and doctors manage diseases. These ongoing efforts

have given rise to a number of novel and proprietary genetic testing services to assist with life-saving health management.

4. Since 2009, Natera has launched ten molecular tests, many of which are available through major health plans accounting for more than 140 million covered persons in the United States. Natera's own robust laboratory processes thousands of genetic tests per month.

5. Natera's pioneering and ongoing innovation is especially evident in the area of cell-free DNA ("cfDNA")-based testing. In the cfDNA field, Natera has developed unique and highly optimized cfDNA-based processes that can be used to test non-invasively for a range of conditions. Natera developed an industry-leading cfDNA test, Panorama, which showcases Natera's mastery of cfDNA in the field of non-invasive diagnostics. Natera's tests are considered the industry leading tests in this space, with over two million tests performed commercially, and with more than twenty-six peer-reviewed publications. Natera has also applied its cfDNA platform to the challenge of detecting and monitoring cancer.

6. In detecting and monitoring cancer, the use of non-invasive, blood-based tests offers significant advantages over older methods, such as invasive tumor biopsy. But the significant technological challenge is that such blood-based testing requires the measurement of very small amounts of relevant genetic material—circulating-tumor DNA ("ctDNA")—within a much larger blood sample. Natera's approach combines proprietary molecular biology and computational techniques to measure genomic variations in tiny amounts of DNA, representing a fundamental advance in molecular biology.

7. Natera has researched and developed cfDNA technology to provide patients and healthcare providers with tools for early, clinically meaningful detection and monitoring of cancer.

8. Natera's cfDNA platform is the product of well over a decade of hard work and investment of, on average, more than fifty million dollars per year in research and development. Natera has expended substantial resources researching and developing its technologies and establishing its reputation among physicians, insurers, and regulators as a company committed to sound science and consistently accurate, reliable results. This research, and the technological innovations resulting therefrom, are protected by a substantial patent portfolio, with over 200 patents issued or pending worldwide, including greater than 60 in the field of oncology.

9. Among these patented inventions are the Asserted Patents, which Inivata infringes. Inivata has used Natera's patented cfDNA technology without permission and in violation of the patent laws.

10. Defendant Inivata, Inc. is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 7020 Kit Creek Road, Suite 140, Research Triangle Park, North Carolina 27560. Defendant Inivata, Inc. is a wholly-owned subsidiary of Defendant Inivata Ltd.

11. Defendant Inivata Ltd. is a corporation organized and existing under the laws of England, having a registered office at The Portway Granta Park, Great Abington, Cambridge, England, CB21 6GS.

12. Both of the Defendants operate under and identify with the trade name "Inivata." Upon information and belief, each of the Defendants directly or indirectly develops, designs, makes, uses, markets, offers to sell and/or sells products and services in the United States, including in the State of Delaware and in this District, and otherwise purposefully directs activities to the same. Upon information and belief, the Defendants have been and are acting in concert and are otherwise liable jointly, severally, or in the alternative for a right to relief with

respect to or arising out of the same transaction, occurrence, or series of transactions or occurrences related to the making, using, offering for sale or selling of at least one infringing product or process.

13. Instead of developing its own science for its cancer detection and monitoring products, Inivata has unlawfully used Natera's patented technology, including in connection with Inivata's InVisionFirst-Lung cancer diagnostic test ("InVisionFirst-Lung") and any other products that use the same or similar technology (collectively, the "Accused Products").

JURISDICTION AND VENUE

14. This Court has subject matter jurisdiction over the matters asserted herein under 28 U.S.C. §§ 1331 and 1338(a).

15. Inivata, Inc. is subject to this Court's personal jurisdiction at least because it is a Delaware corporation. In addition, Defendants are subject to this Court's personal jurisdiction because, on information and belief, Defendants, directly or indirectly, use, offer for sale, and/or sell the Accused Products throughout the United States and within this District. Defendants have infringed and continue to infringe Natera's patents in this District by, among other things, engaging in infringing conduct within and directed at or from this District and purposely and voluntarily placing their infringing products into the stream of commerce with the expectation that the infringing products will be used in this District.

16. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391 and 1400(b) because, among other things, Inivata, Inc. is incorporated in this District, and thus resides in this District, and Inivata Ltd. is not a resident in the United States, and thus may be sued in any Judicial District pursuant to 28 U.S.C. § 1391(c)(3).

BACKGROUND

17. Since 2004, Natera has been a global leader in genetic testing, diagnostics, and DNA testing, including cfDNA testing. Natera's mission is to improve the management of disease worldwide, and it focuses on reproductive health, oncology, and organ transplantation. In pursuit of these goals, Natera has developed novel technologies to make significant and accurate clinical assessments from the miniscule amounts of cfDNA present in a single blood sample. These technologies include methods to manipulate cfDNA in nonconventional ways in order to capture information about genetic variations in cfDNA and usefully transform that information for noninvasive testing.

18. Natera develops and commercializes innovative, non-traditional methods for manipulating and analyzing cfDNA, and offers a host of proprietary cfDNA genetic testing services to the public to assist patients and doctors in evaluating and tracking critical health concerns.

19. Since its founding, Natera has researched, developed, and released ten molecular tests with applications in prenatal diagnostics, cancer, and organ transplants, many of which are available through major health plans, or covered by Medicare or Medicaid, and therefore available to most patients in need of those tests. Natera's tests have helped more than two million people to date. Natera's robust laboratory now processes tens of thousands of tests per month in the United States and internationally, improving the ability of physicians to monitor and manage crucial health issues and patients to prosper around the world.

20. Building on these innovations, in 2017, Natera launched its cfDNA diagnostic test to detect and monitor cancer, called Signatera®. Signatera® is a personalized ctDNA surveillance tool that detects molecular residual disease ("MRD") when assessing disease recurrence or treatment response in solid tumors. Signatera® is designed to screen for multiple

tumor-derived targets with each assay. It is optimized to detect extremely low quantities of ctDNA and provides early knowledge of disease recurrence with a >99.5% clinical test specificity.

21. MRD assessment has become a standard of care in the management of patients with hematological malignancies, but until recently it has not been possible in solid cancers due to technical limitations. Accurate MRD testing and molecular monitoring offers the potential for physicians to change or escalate treatment in patients who are MRD-positive, and to de-escalate or avoid unnecessary treatment in patients who are MRD-negative. It also holds potential as a surrogate endpoint in clinical trials.

22. Natera's technology has been validated in multiple clinical studies. In Cancer Research UK/University College London's Tracking Cancer Evolution through Therapy ("TRACERx"), Natera's technology was used for the multi-year monitoring of patient-specific single-nucleotide variants (SNVs) in plasma, to understand the evolution of cancer mutations over time, and to monitor patients for disease recurrence. Results from the first 100 early-stage lung cancer patients analyzed as part of the study were featured on the cover of the May 2017 issue of Nature and showed that an early prototype version of Signatera® identified 43% more ctDNA-positive early-stage lung cancer cases than a generic lung cancer panel and demonstrated its potential to detect residual disease, measure treatment response, and identify recurrence up to 11 months earlier than the standard of care, with a sensitivity of 93% at time of relapse.

23. Natera has also collaborated with Aarhus University in Denmark, Imperial College London, University of Leicester, Institute Jules Bordet, Fox Chase Cancer Center, University of California, San Francisco, and Foundation Medicine, Inc with respect to cancer research.

24. The U.S. Food and Drug Administration ("FDA") recognized the importance of Natera's Signatera® and granted it "Breakthrough Device" designation on May 6, 2019. That designation will help accelerate FDA assessment and review of Signatera® as an in vitro diagnostic for use in pharmaceutical trials.

25. Signatera®'s validation has also led Medicare to issue a draft Local Coverage Determination ("LCD") for Signatera® in March 2019. In its draft LCD, Medicare determined that "[t]he analytical validity and clinical validity of minimal residual disease testing using cell-free DNA, and Signatera® in particular, appears to be well established based on available information for the test."

26. The Asserted Patents resulted from Natera's years-long research in developing innovative new methods for amplifying and sequencing cell-free DNA.

General Background of the Inventions

27. The '755 patent, attached hereto as Exhibit 1, is entitled "Detecting Cancer Mutations and Aneuploidy in Chromosomal Segments" and issued from the United States Patent and Trademark Office ("USPTO") on April 16, 2019. Natera owns the '755 patent, including the right to enforce it and seek damages for infringement.

28. The '755 patent claims methods for detecting genetic mutations, including aneuploidy, in tumor DNA. Independent claim 1 of the '755 patent recites:

> A method for determining the genetic mutations in a solid tumor from an individual, comprising:
>
> A. determining whether an aneuploidy mutation is present by analyzing a sample of blood or a fraction thereof from the individual to determine a level of allelic imbalance for each of a plurality of chromosomes or chromosome segments known to exhibit aneuploidy in cancer by:
>
> isolating circulating tumor DNA from a blood sample, serum sample, or plasma sample from the individual,

amplifying at least 1000 polymorphic loci relating to cancer-associated aneuploidy from each of the plurality of chromosomes or chromosome segments of the circulating tumor DNA to obtain amplicons,

generating nucleic acid sequence data for a set of polymorphic loci on each of the plurality of chromosomes or chromosome segments by performing high throughput DNA sequencing of the amplicons,

using the nucleic acid sequence data to generate phased allelic data for the set of polymorphic loci on each of the plurality of chromosomes or chromosome segments, and

determining the level of allelic imbalance for each of the plurality of chromosomes or chromosome segments using the phased allelic data, wherein a detectable allelic imbalance is indicative of an aneuploidy mutation in the solid tumor for each of the plurality of chromosomal segments; and

B. determining whether a single nucleotide variant is present in a plurality of single nucleotide variant loci known to be associated with cancer by:

isolating circulating tumor DNA from a blood sample, serum sample, or plasma sample from the individual,

amplifying a plurality of polymorphic loci relating to cancer-associated single nucleotide variance loci from each of the plurality of chromosomes or chromosome segments of the circulating tumor DNA to obtain amplicons, and

performing high throughput DNA sequencing of the amplicons, wherein the presence of the single nucleotide variant in the sample for any of the plurality of single nucleotide loci is indicative of the presence of the single nucleotide variant in the solid tumor, thereby determining the genetic mutations in the solid tumor.

29. The ’709 patent, attached hereto as Exhibit 2, is entitled “Methods for Simultaneous Amplifications of Target Loci” and issued from the USPTO on March 24, 2020. Natera owns the ’709 patent, including the right to enforce it and seek damages for infringement.

30. The ’709 patent claims methods for simultaneously amplifying multiple nucleic acid regions of interest in a reaction mixture. The claimed methods amplify the nucleic acids under particular reaction conditions and sequence the nucleic acids. Independent claim 1 of the ’709 patent recites:

A method of amplifying target loci in a nucleic acid sample, the method comprising:

contacting the nucleic acid sample comprising at least 50 target loci with a library of at least 50 different primers to produce a reaction mixture;

subjecting the reaction mixture to primer extension reaction conditions to produce amplified products comprising target amplicons; wherein the annealing temperature for the reaction conditions is greater than a melting temperature of the at least 50 primers, and wherein the at least 50 of the target loci are simultaneously amplified; and sequencing the amplified products.

The '755 Patent Is Not Directed To A Natural Phenomenon And Its Steps Were Not Routine Or Conventional

31. The claims of the '755 patent are not directed to an abstract idea, natural law, or natural phenomenon. Rather, they are directed to a nonconventional, non-routine technique for measuring DNA in a sample using synthetic pieces of DNA, including amplification products, which are produced using synthetic tools such as primers, to provide a specific, innovative solution to issues peculiar to the particular problem of amplifying and measuring small amounts of DNA from a solid tumor in a biological sample of an individual. Moreover, the claims of the '755 patent cover methods of preparation. Analogous claims were held to not be directed to a natural law or phenomenon in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, No. 2019-1419, 2020 WL 1264002 (Fed. Cir. Mar. 17, 2020).

32. The '755 patent claims are directed to specific, nonconventional, non-routine methods for overcoming previously unresolved problems in this area. For example, as of the date of the invention, it would not have been routine or conventional to perform the claimed techniques either individually or in combination, including: amplifying at least 1,000 polymorphic loci relating to cancer-associated aneuploidy from one or more chromosomes or chromosome segments of circulating tumor DNA to obtain amplicons, generating nucleic acid sequence data for a set of polymorphic loci on each of the plurality of chromosomes or chromosome segments by performing high throughput DNA sequencing of the amplicons, using the nucleic acid sequence data to generate phased allelic data for the set of polymorphic loci on

each of the plurality of chromosomes or chromosome segments, and determining the level of allellic imbalance for each of the plurality of chromosomes or chromosome segments using the phased allelic data, as well as amplifying a plurality of polymorphic loci relating to cancer-associated single nucleotide variance loci from each of the plurality of chromosomes or chromosome segments of the circulating tumor DNA to obtain amplicons and performing high throughput DNA sequencing of the amplicons, in the context of the invention.

The ’709 Patent Is Not Directed To A Natural Phenomenon And Its Steps Were Not Routine Or Conventional

33. The claims of the ’709 patent are not directed to an abstract idea, natural law, or natural phenomenon. Rather, they are directed to an innovative method of sample preparation comprising amplifying and sequencing nucleic acid samples using synthetic primers and amplification products to provide a novel and innovative solution to issues peculiar to the particular problem of amplifying and sequencing small amounts of nucleic acid samples. The claims of the ’709 patent cover methods of preparation of an unnatural preparation. Analogous claims were held to not be directed to a natural law or phenomenon, for example, in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, No. 2019-1419, 2020 WL 1264002 (Fed. Cir. Mar. 17, 2020).

34. The ’709 patent claims are directed to specific, nonconventional, non-routine methods for overcoming previously unresolved problems in this area. For example, as of the date of the invention, it would not have been routine or conventional to perform the claimed techniques either individually or in combination, including: contacting a nucleic acid sample comprising at least 50 target loci with a library of at least 50 different primers to produce a reaction mixture, subjecting the reaction mixture to primer extension reaction conditions to produce amplified products comprising target amplicons, wherein the annealing temperature for

the reaction conditions is greater than a melting temperature of the at least 50 primers, and wherein the at least 50 of the target loci are simultaneously amplified, and sequencing the amplified products, in the context of the invention.

INIVATA'S INFRINGING ACTS

35. The allegations provided below are exemplary and without prejudice to Natera's infringement contentions. In providing these allegations, Natera does not convey or imply any particular claim constructions or the precise scope of the claims. Natera's claim construction contentions regarding the meaning and scope of the claim terms will be provided under the Court's scheduling order and local rules.

36. The infringing products include, but are not limited to, InVisionFirst-Lung, and any other infringing method, product, device, or test developed by Inivata that apply Natera's patented methods for preparing, amplifying, sequencing, and analyzing cfDNA to detect and monitor genes and genetic mutations commonly associated with cancers.

37. As provided in more detail below, each element of at least one claim of the Asserted Patents is literally present in InVisionFirst-Lung or is literally practiced by the processes through which InVisionFirst-Lung is practiced. To the extent that any element is not literally present or practiced, each such element is present or practiced under the doctrine of equivalents.

38. Attached as Exhibit 3 is a preliminary and exemplary claim chart describing Inivata's infringement of claim 1 of the '755 patent. Exhibits 5 to 10 are documents referenced in the Exhibit 3 chart, which demonstrate examples of Inivata's infringement. The claim chart is not intended to limit Natera's right to modify the chart or allege that other products or activities of Inivata infringe the identified claim or any other claims of the '755 patent or any other patents. Inivata infringes more than one claim of the '755 patent.

39. Exhibit 3 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 3 that is mapped to the Accused Products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure, and therefore a response to each claim element is required.

40. Attached as Exhibit 4 is a preliminary and exemplary claim chart describing Inivata's infringement of claim 1 of the '709 patent. Exhibits 6-7A, 10-10A are documents referenced in the Exhibit 4 chart, which demonstrate examples of Inivata's infringement. The claim chart is not intended to limit Natera's right to modify the chart or allege that other products or activities of Inivata infringe the identified claim or any other claims of the '709 patent or any other patents. Inivata infringes more than one claim of the '709 patent.

41. Exhibit 4 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 4 that is mapped to the Accused Products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure, and therefore a response to each claim element is required.

42. Inivata began selling and offering to sell InVisionFirst-Lung in the United States on or about June 29, 2020, including through NeoGenomics, Inc., Inivata's strategic commercialization partner in the United States.

43. Inivata has its own CLIA-certified laboratory in the United States that has performed and/or will perform one or more of the Accused Products.

44. Inivata is a direct competitor of Natera in the market for recurrence monitoring for cancer, including lung cancer.

45. Inivata has actual knowledge of the '755 patent since at least as early as the date of this Complaint.

46. Inivata has actual knowledge of the '709 patent since at least as early as the date of this Complaint.

47. Inivata has thus made extensive use of Natera's patented technology, including the technology described and claimed in the '755 patent and the '709 patent. Natera has no choice but to defend its proprietary and patented technology. Natera thus requests that this Court award it damages sufficient to compensate for Inivata's infringement of the '755 patent and the '709 patent, find this case exceptional, award Natera its attorneys' fees and costs, and grant an injunction against Inivata to prevent ongoing infringement of the '755 patent and the '709 patent.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 10,262,755

48. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

49. Natera is the owner of the '755 patent, which was duly and legally issued by the USPTO on April 16, 2019.

50. Inivata has infringed and continues to infringe at least one claim of the '755 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by performing within the United States and without authority the tests of the Accused Products.

51. Inivata's infringement has damaged and will continue to damage Natera, which is entitled to recover the damages resulting from Inivata's wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

52. Moreover, Inivata's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless Inivata is enjoined from any and all activities that would infringe the claims of the '755 patent.

COUNT II: INFRINGEMENT OF U.S. PATENT NO. 10,597,709

53. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

54. Natera is the owner of the '709 patent, which was duly and legally issued by the USPTO on March 24, 2020.

55. Inivata has infringed and continues to infringe at least one claim of the '709 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by performing within the United States and without authority the tests of the Accused Products.

56. Inivata's infringement has damaged and will continue to damage Natera, which is entitled to recover the damages resulting from Inivata's wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

57. Moreover, Inivata's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless Inivata is enjoined from any and all activities that would infringe the claims of the '709 patent.

PRAYER FOR RELIEF

WHEREFORE, Natera respectfully requests the following relief:

1. A judgment that Inivata has infringed the Asserted Patents literally or under the doctrine of equivalents;

2. An order enjoining Inivata and its officers, directors, agents, servants, affiliates, employees, divisions, branches, subsidiaries, parents, and all others acting on behalf of or in active concert or participation therewith, from further infringement of the Asserted Patents;

3. An award of damages sufficient to compensate Natera for Inivata's infringement under 35 U.S.C. § 284;

4. A determination that this is an exceptional case under 35 U.S.C. § 285 and that Natera be awarded attorneys' fees;

5. Costs and expenses in this action;

6. An award of prejudgment and post-judgment interest; and

7. Such other and further relief as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Natera respectfully demands a trial by jury on all triable issues.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

Jack B. Blumenfeld (#1014)
Derek J. Fahnestock (#4705)
Anthony D. Raucci (#5948)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@mnat.com
dfahnestock@mnat.com
araucci@mnat.com

Attorneys for Plaintiff Natera, Inc.

OF COUNSEL:

Kevin P.B. Johnson
Victoria F. Maroulis
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
555 Twin Dolphin Shores
Redwood Shores, CA 94065
(650) 801-5000

Sam S. Stake
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
50 California Street, 22nd Floor
San Francisco, CA 94111
(415) 875-6600

Sandra Haberny, Ph.D.
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
865 South Figueroa Street, 10th Floor
Los Angeles, CA 90017
(213) 443-3000

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